Prolonged stress is considered to be one of the major triggers of depression – a multifaceted illness associated with impairments of the homeostatic control of neural activity in different brain circuits. Nevertheless, many people and laboratory animals exposed to a challenging conditions maintain normal behavior and, in the case of humans, cognitive flexibility and optimism. These subjects are described as being resilient to stress. Numerous scientific and clinical studies have been performed to explain the pathological changes underlying the depression. However, only a few studies have focused on the molecular and neurobiological mechanisms of the stress-resilience phenomenon. Genetic and epigenetic factors profoundly contribute to dynamic responses to stress. RNA interference phenomenon controls homeostasis of the brain and its adaptive capacity and thus seem to be very appealing system for search of new potential markers of the stress resilience and susceptibility. RNA interference (RNAi) is an epigenetic process showing astonishingly low rate of evolution which is broadly observed among plants and animals. RNAi regulates gene expression using small and non-coding RNA transcripts. In eukaryotes, including mammals, microRNAs (miRNAs) are a class of endogenous small RNAs (17-22 nucleotides) responsible for sequence-specific and posttranscriptional regulation of more than 70% of genes. Additionally its conservation among mammals create great opportunity to translate scientific results into clinical studies. Thus the aim of the present project is to investigate the role of miRNA biogenesis system in response to stress. The project is based on using chronic mil stress paradigm – a validated, preclinical model of depression which allows to differentiate animals being less vulnerable to stress than others which is analogous to a heterogeneous human population. Identification of biochemical markers of stress-resilience and of vulnerability to stress is of prime importance for understanding disease mechanisms for the depression which, despite extensive and longitudinal studies, are not fully understood. In this project we will attempt identification of potential factors differentiating stress resilient subjects from susceptible ones at different levels of miRNA biogenesis system what may be a prelude for new therapeutic targets acting at the level of miRNA processing proteins.